

REMARKS/ARGUMENTS

Claims 21-35 are pending, claims 25-35 having been withdrawn from consideration. By this Amendment, claims 21-24 are amended. Support for the amendments to claims 21-24 can be found, for example, in original claims 21-24. The amendments to claims 21-24 are made solely to improve their clarity. No new matter is added. In view of the foregoing amendments and following remarks, reconsideration and allowance are respectfully requested.

Personal Interview

Applicants appreciate the courtesies extended to Applicants' representative by Examiners Palenik and Woodward during the June 5, 2008 Personal Interview. Applicants' separate record of the substance of the interview is incorporated in the following remarks.

Withdrawn Claims

For the reasons set forth below, Applicants submit that all pending claims presently subject to examination are in condition for allowance. Because the withdrawn claims depend from, and thus recite all features of, allowable claim 1, rejoinder and allowance of the withdrawn claims are respectfully requested.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Office Action rejects claims 21-24 as indefinite under 35 U.S.C. §112, second paragraph. Applicants respectfully traverse the rejection.

The Office Action asserts that the phrase "extremely poorly water-soluble drug" is indefinite. While Applicants do not necessarily agree, claim 21 is amended to specify that

"the extremely poorly water-soluble drug has a solubility in water at 25 °C of less than 10 µg/mL prior to treatment."

For the foregoing reasons, claims 21-24 are definite. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection Under 35 U.S.C. §102

The Office Action rejects claims 21-24 under 35 U.S.C. §102(b) over U.S. Patent No. 6,348,468 to Ohkuchi et al. ("Ohkuchi"). Applicants respectfully traverse the rejection.

Claim 1 recites "[a] composition, comprising: an extremely poorly water-soluble drug; and a porous silica material; wherein: the composition is obtained by treating a mixture comprising the porous silica material and the extremely poorly water-soluble drug with a supercritical fluid or subcritical fluid of carbon dioxide; the extremely poorly water-soluble drug has a solubility in water at 25 °C of less than 10 µg/mL prior to treatment; the porous silica material has an average pore diameter in a range of from 1 to 20 nm, where pores having diameters within  $\pm 40\%$  of the average pore size account for at least 60% of a total pore volume of the porous silica material, and the porous silica material has an X-ray diffraction spectrum including at least one peak at a position of diffraction angle ( $2\theta$ ) corresponding to a  $d$  value of at least 1 nm" (emphasis added). Ohkuchi does not disclose or suggest such a composition.

As indicated above, claim 21 requires that the composition be obtained by treating a mixture comprising an extremely poorly water-soluble drug and a porous silica material with a supercritical or subcritical carbon dioxide fluid. The Office Action asserts that Ohkuchi discloses a composition including 5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2-benzyl-2H-pyridazin-3-one, corresponding to the extremely poorly water-soluble drug of claim 21. *See*

Office Action, page 5. The Office Action asserts that the product-by-process step of claim 21, emphasized above, should not be given patentable weight. *See* Office Action, page 4.

At the outset, Applicants note that claim 21 expressly recites a porous silica material, which is neither disclosed nor suggested by Ohkuchi. Also, while the patentability of a product does not depend on its method of production, the structure implied by process steps should be considered when assessing patentability. *See* MPEP §2114. In this case, Applicants have demonstrated that treating a mixture comprising an extremely poorly water-soluble drug and a porous material with a supercritical or subcritical carbon dioxide fluid greatly improves the solubility of the extremely poorly water-soluble drug. *See, e.g.*, present specification, page 29, Table 1 (compare Examples 1 and 2 and Comparative Examples 1 and 2). As the composition of claim 21 has different properties than compositions such as in Ohkuchi, the compositions of Ohkuchi cannot be said to anticipate or render obvious the composition of claim 21.

As explained, claim 21 is not anticipated by Ohkuchi. Claims 22-24 depend from claim 1 and, thus, also are not anticipated by Ohkuchi. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

#### Rejection Under 35 U.S.C. §103

The Office Action rejects claims 21-24 under 35 U.S.C. §103(a) over WO 02/20624 to Mandel et al. ("Mandel") in view of JP 2002-345940 to Nakanishi et al. ("Nakanishi"), Ohkuchi and Sigma-Aldrich Silica Gel Product No. 403653 ("Sigma-Aldrich"). Applicants respectfully traverse the rejection.

Claim 21 is set forth above. Mandel, Nakanishi, Ohkuchi and Sigma-Aldrich do not disclose or suggest such a composition.

As indicated above, claim 21 requires that the composition be obtained by treating a mixture comprising an extremely poorly water-soluble drug and a porous material with a supercritical or subcritical carbon dioxide fluid. As conceded in the Office Action, none of the cited references discloses a composition including these particular components produced in this particular manner. *See* Office Action, pages 6 to 8. Mandel and Nakanishi are directed to methods of preparing slow- or sustained-release compositions. *See* Mandel, Abstract; Nakanishi, Abstract. That is, Mandel and Nakanishi are directed to methods of reducing or delaying the solubility of active ingredients. *See, e.g.,* Mandel, page 1, lines 14 to 15. Ohkuchi, by contrast, is relied on for its disclosure of compounds, such as 5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2-benzyl-2H-pyridazin-3-one (*see* Ohkuchi, column 33, lines 14 to 27), which have extremely poor water solubility (*see* present specification, page 6, lines 17 to 21). To combine the teachings of Mandel, Nakanishi and Ohkuchi, would involve attempting to make an active ingredient already having extremely poor solubility even less soluble. One of ordinary skill in the art would not have been motivated to combine the references as proposed in the Office Action. *See, e.g.,* MPEP §2143.01.

Sigma-Aldrich is cited for its alleged disclosure of silicas having particular properties. *See* Office Action, page 8. However, the teachings of Sigma-Aldrich do not overcome the deficiencies of the combined teachings of Mandel, Nakanishi and Ohkuchi, as outlined above.

For the reasons discussed above, a *prima facie* case of obviousness has not been made. However, even if a *prima facie* case were made, such case is rebutted by the results shown in the present specification – "[a] *prima facie* case of obviousness ... is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties." *See* MPEP §2144.09 (citing *In re Papesch*, 315 F.2d 381 (C.C.P.A. 1963)). The Examples of the present specification demonstrate that compositions, such as recited in claim

21, provide superior dissolution properties relative to known compositions, which are not produced by treating a mixture comprising an extremely poorly water-soluble drug and a porous material with a supercritical or subcritical carbon dioxide fluid. *See, e.g.*, present specification, page 29, Table 1. These results are objective evidence of the improvements of the composition of claim 21 over known compositions, and thus these results rebut any suggestion that it would have been obvious to combine the teachings of Mandel, Nakanishi, Ohkuchi and Sigma-Aldrich as proposed in the Office Action.

As explained, claim 21 would not have been rendered obvious by Mandel, Nakanishi, Ohkuchi and Sigma-Aldrich. Claims 22-24 depend from claim 1 and, thus, also would not have been rendered obvious by Mandel, Nakanishi, Ohkuchi and Sigma-Aldrich. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

#### Double Patenting

The Office Action provisionally rejects claims 21-24 under the judicially created doctrine of obviousness-type double patenting over claims 1, 8, 11 and 12 of U.S. Patent Application No. 10/551,901. Applicants respectfully traverse the rejection.

Claim 21 of the present application recites that "the porous silica material has an average pore diameter in a range of from 1 to 20 nm, where pores having diameters within  $\pm 40\%$  of the average pore size account for at least 60% of a total pore volume of the porous silica material, and the porous silica material has an X-ray diffraction spectrum including at least one peak at a position of diffraction angle ( $2\theta$ ) corresponding to a  $d$  value of at least 1 nm" (emphasis added). Claim 1 of the 901 application, by contrast, recites that "the porous material is not a porous silica material having an average pore diameter of 1 to 20 nm, where a total pore volume of pores having a diameter falling within a range of  $\pm 40\%$  of the average pore diameter accounts for 60% or more of a volume of all of the pores of the porous

material, and having an X-ray diffraction spectrum including one or more peaks at a diffraction angle ( $2\theta$ ) corresponding to d of 1 nm or more" (emphasis added). The porous materials of the claims of the present application and the porous materials of the claims of the 901 application do not overlap and, thus, the claims of 901 application cannot render obvious the claims of the present application.

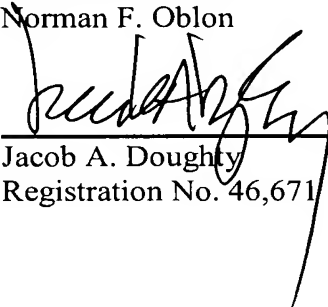
Accordingly, claims 21-24 of the present application are not obvious over claims 1, 8, 11 and 12 of the 901 application. Reconsideration and withdrawal of the rejection are respectfully requested.

#### Conclusion

For the foregoing reasons, Applicants submit that claims 21-35 are in condition for allowance. Prompt reconsideration and allowance are respectfully requested.

Respectfully submitted,

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